☐ 1: BAA24942. Reports CFTR [Oryctolagus...[gi:2911137] BLink, Links

Comment Features Sequence

```
LOCUS       BAA24942                30 aa            linear   MAM 14-APR-2000
DEFINITION  CFTR [Oryctolagus cuniculus].
ACCESSION   BAA24942
VERSION     BAA24942.1  GI:2911137
DBSOURCE    accession AB011005.1
KEYWORDS    .
SOURCE      Oryctolagus cuniculus (rabbit)
  ORGANISM  Oryctolagus cuniculus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Glires; Lagomorpha;
            Leporidae; Oryctolagus.
REFERENCE   1
  AUTHORS   Yajima,T., Matsuoka,R. and Kawana,M.
  TITLE     Rabbit CFTR exon 5
  JOURNAL   Published Only in Database (1998)
REFERENCE   2  (residues 1 to 30)
  AUTHORS   Yajima,T., Matsuoka,R. and Kawana,M.
  TITLE     Direct Submission
  JOURNAL   Submitted (07-FEB-1998) Toshitaka Yajima, Tokyo Women's Medical
            College, The Heart Institute of Japan; Kawada-cho 8-1, Shinjuku-ku,
            Tokyo 162, Japan (E-mail:yajiyaji@246.ne.jp, Tel:81-3-3353-8111,
            Fax:81-3-3356-0441)
COMMENT     On Feb 25, 1998 this sequence version replaced gi:2897735.
            Sequence updated (19-Feb-1998).
FEATURES             Location/Qualifiers
     source          1..30
                     /organism="Oryctolagus cuniculus"
                     /db_xref="taxon:9986"
                     /tissue_type="heart"
     Protein         1..30
                     /name="CFTR"
     CDS             1..30
                     /gene="CFTR"
                     /coded_by="AB011005.1:<1..>90"
ORIGIN
        1 tlkpssrvld kisigqlisl lsnnlnkfde
//
```

☐ **1:** AAA73561 Reports BLink, Links
CFTR gene product
gi|915270|gb|AAA73561.1|[915270]

☐ **2:** CAB37191 Reports BLink, Conserved Domains, Links
CFTR [Rattus norvegicus]
gi|4456765|emb|CAB37191.1|[4456765]

☐ **3:** CAA65168 Reports BLink, Links
CFTR [Rattus norvegicus]
gi|1707662|emb|CAA65168.1|[1707662]

☐ **4:** AAB24879 Reports BLink, Conserved Domains, Links
cystic fibrosis transmembrane conductance regulator, CFTR [rats, parotid gland, Peptide Partial, 512 aa]
gi|263318|gb|AAB24879.1||bbm|270246|bbs|122312[263318]

☐ **5:** P34158_2 Reports BLink, Conserved Domains, Links
[Segment 2 of 2] Cystic fibrosis transmembrane conductance regulator (CFTR) (cAMP-dependent chloride channel) (ATP-binding cassette transporter sub-family C member 7)
gi|21431744|sp||P34158_2[21431744]

☐ **6:** P34158_1 Reports BLink, Links
[Segment 1 of 2] Cystic fibrosis transmembrane conductance regulator (CFTR) (cAMP-dependent chloride channel) (ATP-binding cassette transporter sub-family C member 7)
gi|21431743|sp||P34158_1[21431743]

☐ **7:** P34158 Reports BLink, Links
Cystic fibrosis transmembrane conductance regulator (CFTR) (cAMP-dependent chloride channel) (ATP-binding cassette transporter sub-family C member 7)
gi|21431742|sp|P34158|CFTR_RAT[21431742]

☐ **8:** NP_113694 Reports BLink, Conserved Domains, Links
cystic fibrosis transmembrane conductance regulator homolog [Rattus norvegicus]
gi|91982740|ref|NP_113694.1|[91982740]

☐ **9:** XP_001059206 Reports BLink, Conserved Domains, Links

PREDICTED: similar to cystic fibrosis transmembrane conductance regulator homolog [Rattus norvegicus]
gi|109473187|ref|XP_001059206.1|[109473187]

☐ **10:** Reports BLink, Conserved Domains, Links
XP_001062374
PREDICTED: similar to cystic fibrosis transmembrane conductance regulator homolog [Rattus norvegicus]
gi|109471801|ref|XP_001062374.1|[109471801]

☐ **11:** Reports BLink, Conserved Domains, Links
AAA40918
cystic fibrosis transmembrane conductance regulator
gi|203423|gb|AAA40918.1|[203423]

☐ **12:** Reports BLink, Conserved Domains, Links
AAR16315
cystic fibrosis transmembrane conductance regulator, ATP-binding cassette (sub-family C, member 7) [Rattus norvegicus]
gi|38322765|gb|AAR16315.1|[38322765]

☐ **13:** Reports BLink, Conserved Domains, Links
NP_066388
cystic fibrosis transmembrane conductance regulator homolog [Mus musculus]
gi|14141185|ref|NP_066388.1|[14141185]

☐ **14:** P26361 Reports BLink, Conserved Domains, Links
Cystic fibrosis transmembrane conductance regulator (CFTR) (cAMP-dependent chloride channel) (ATP-binding cassette transporter sub-family C member 7)
gi|20141218|sp|P26361|CFTR_MOUSE[20141218]

☐ **15:** Reports BLink, Conserved Domains, Links
NP_036784
solute carrier family 9, member 1 [Rattus norvegicus]
gi|6981558|ref|NP_036784.1|[6981558]

☐ **16:** Reports BLink, Conserved Domains, Links
NP_445876
solute carrier family 4, sodium bicarbonate cotransporter, member 4 [Rattus norvegicus]
gi|16758164|ref|NP_445876.1|[16758164]

☐ **17:** Reports BLink, Conserved Domains, Links
NP_036786
solute carrier family 9, member 3 [Rattus norvegicus]
gi|6981562|ref|NP_036786.1|[6981562]

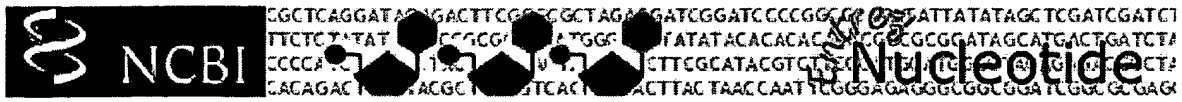
☐ **18:** Reports BLink, Conserved Domains, Links
NP_113736
sodium channel, nonvoltage-gated, type I, alpha polypeptide [Rattus norvegicus]
gi|13928742|ref|NP_113736.1|[13928742]

☐ **19:** 1901178A Reports BLink, Conserved Domains, Links
cystic fibrosis transmembrane conductance regulator
gi|382755|prf||1901178A[382755]

☐ **20:** Q9R1N3 Reports BLink, Conserved Domains, Links
Sodium bicarbonate cotransporter 3 (Electroneutral sodium bicarbonate cotransporter 1) (NBC-like protein) (Solute carrier family 4 member 7)
gi|81869688|sp|Q9R1N3|S4A7_RAT[81869688]

Items 1 - 20 of 72 Page 1 of 4 Next
Display Summary Show 20 Sort by Relevance Send to

Sep 25 2006 08:46:41



1: AB011005. Reports Oryctolagus cunic...[gi:2911136]

Links

Comment Features Sequence

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LOCUS       AB011005                  90 bp    mRNA    linear   MAM 14-APR-2000
DEFINITION  Oryctolagus cuniculus CFTR mRNA, exon 5, partial cds.
ACCESSION   AB011005
VERSION     AB011005.1  GI:2911136
KEYWORDS    CFTR.
SOURCE      Oryctolagus cuniculus (rabbit)
  ORGANISM  Oryctolagus cuniculus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Glires; Lagomorpha;
            Leporidae; Oryctolagus.
REFERENCE   1
  AUTHORS   Yajima,T., Matsuoka,R. and Kawana,M.
  TITLE     Rabbit CFTR exon 5
  JOURNAL   Published Only in Database (1998)
REFERENCE   2  (bases 1 to 90)
  AUTHORS   Yajima,T., Matsuoka,R. and Kawana,M.
  TITLE     Direct Submission
  JOURNAL   Submitted (07-FEB-1998) Toshitaka Yajima, Tokyo Women's Medical
            College, The Heart Institute of Japan; Kawada-cho 8-1, Shinjuku-ku,
            Tokyo 162, Japan (E-mail:yajiyaji@246.ne.jp, Tel:81-3-3353-8111,
            Fax:81-3-3356-0441)
COMMENT     On Feb 25, 1998 this sequence version replaced gi:2897734.
            Sequence updated (19-Feb-1998).
FEATURES             Location/Qualifiers
     source          1..90
                     /organism="Oryctolagus cuniculus"
                     /mol_type="mRNA"
                     /db_xref="taxon:9986"
                     /tissue_type="heart"
     gene            <1..>90
                     /gene="CFTR"
     CDS             <1..>90
                     /gene="CFTR"
                     /codon_start=1
                     /protein_id="BAA24942.1"
                     /db_xref="GI:2911137"
                     /translation="TLKPSSRVLDKISIGQLISLLSNNLNKFDE"
     exon            1..90
                     /gene="CFTR"
                     /number=5
ORIGIN
        1 actttaaagc cgtcaagccg tgttctagat aaaataagta ttgggcaact tattagtctc
       61 ctttccaaca acctgaacaa atttgatgaa
//
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Sep 27 2006 15:22:06

☐ 1: CAA65168. Reports CFTR [Rattus norv...[gi:1707662] BLink, Links

Features Sequence

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LOCUS       CAA65168                 18 aa            linear   ROD 20-SEP-1999
DEFINITION  CFTR [Rattus norvegicus].
ACCESSION   CAA65168
VERSION     CAA65168.1  GI:1707662
DBSOURCE    embl locus RNCFTR7, accession X95927.1
KEYWORDS    .
SOURCE      Rattus norvegicus (Norway rat)
  ORGANISM  Rattus norvegicus
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia;
            Sciurognathi; Muroidea; Muridae; Murinae; Rattus.
REFERENCE   1
  AUTHORS   Vuillaumier,S., Kaltenboeck,B., Lecointre,G., Lehn,P. and
            Denamur,E.
  TITLE     Phylogenetic analysis of cystic fibrosis transmembrane conductance
            regulator gene in mammalian species argues for the development of a
            rabbit model for cystic fibrosis
  JOURNAL   Mol. Biol. Evol. 14 (4), 372-380 (1997)
   PUBMED   9100367
REFERENCE   2  (residues 1 to 18)
  AUTHORS   Vuillaumier,S.
  TITLE     Direct Submission
  JOURNAL   Submitted (27-FEB-1996) S. Vuillaumier, INSERM U120, 48 Boulevard
            Serrurier, Paris, F-75019, FRANCE
FEATURES             Location/Qualifiers
     source          1..18
                     /organism="Rattus norvegicus"
                     /db_xref="taxon:10116"
                     /chromosome="7"
     Protein         1..18
                     /name="CFTR"
     CDS             1..18
                     /gene="CFTR"
                     /coded_by="X95927.1:2284..2340"
                     /db_xref="UniProtKB/TrEMBL:P97522"
ORIGIN
        1 mqksplekas fisklffr
//
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☐ 1: AAB46752. Reports cystic fibrosis t...[gi:7545193]

BLink, Conserved Domains, Links

Comment Features Sequence

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LOCUS       AAB46752                269 aa            linear   MAM 12-APR-2000
DEFINITION  cystic fibrosis transmembrane conductance regulator; CFTR [Mustela
            putorius furo].
ACCESSION   AAB46752
VERSION     AAB46752.2  GI:7545193
DBSOURCE    accession S82688.1
KEYWORDS    .
SOURCE      Mustela putorius furo (domestic ferret)
  ORGANISM  Mustela putorius furo
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Laurasiatheria; Carnivora; Caniformia;
            Mustelidae; Mustelinae; Mustela.
REFERENCE   1  (residues 1 to 269)
  AUTHORS   Sehgal,A., Presente,A. and Engelhardt,J.F.
  TITLE     Developmental expression patterns of CFTR in ferret tracheal
            surface airway and submucosal gland epithelia
  JOURNAL   Am. J. Respir. Cell Mol. Biol. 15 (1), 122-131 (1996)
   PUBMED   8679216
  REMARK    GenBank staff at the National Library of Medicine created this
            entry [NCBI gibbsq 179002] from the original journal article.
COMMENT     On Apr 12, 2000 this sequence version replaced gi:1835882.
            Method: conceptual translation supplied by author.
FEATURES             Location/Qualifiers
     source          1..269
                     /organism="Mustela putorius furo"
                     /sub_species="furo"
                     /db_xref="taxon:9669"
                     /tissue_type="lung"
     Protein         <1..>269
                     /product="cystic fibrosis transmembrane conductance
                     regulator"
                     /note="CFTR"
     Region          47..>269
                     /region_name="ABC_CFTR1_C"
                     /note="The CFTR subfamily domain 1; cd03291"
                     /db_xref="CDD:48324"
     Region          109..269
                     /region_name="ABC_tran"
                     /note="ABC transporter; pfam00005"
                     /db_xref="CDD:40107"
     CDS             1..269
                     /gene="CFTR"
                     /coded_by="S82688.1:<1..>808"
                     /note="conceptual translation presented here differs from
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                  translation in publication"
ORIGIN
        1 civlrmavtr qfpwavqtwy dslgainkiq dflqkqeykt leynltttev vmenvtafwe
       61 egfgelleka kqnsndrkxs nadnslffsn fsllgapvlk disfkiergq llavagstga
      121 gktsllmmim gelepsegki khsgrisfcs qfswimpgti keniifgvsy deyryrsvik
      181 acqleedisk faekdnivlg eggitlsggq rarislarav ykdadlylld spfgyldvlt
      241 ekeifescvc klmanktril vtskmehlk
//
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☐ 1: AAB20219. Reports cystic fibrosis t...[gi:7705025] Links

Comment Features Sequence

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LOCUS       AAB20219                  10 aa            linear   PRI 04-MAY-2000
DEFINITION  cystic fibrosis transmembrane conductance regulator; CFTR [Homo
            sapiens].
ACCESSION   AAB20219
VERSION     AAB20219.2  GI:7705025
DBSOURCE    accession S64643.1
KEYWORDS    .
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
            Catarrhini; Hominidae; Homo.
REFERENCE   1  (residues 1 to 10)
  AUTHORS   Schwarz,M., Summers,C., Heptinstall,L., Newton,C., Markham,A. and
            Super,M.
  TITLE     A deletion mutation of the cystic fibrosis transmembrane
            conductance regulator (CFTR) locus: Delta I507
  JOURNAL   Adv. Exp. Med. Biol. 290, 393-398 (1991)
   PUBMED   1719770
  REMARK    GenBank staff at the National Library of Medicine created this
            entry [NCBI gibbsq 64648] from the original journal article.
COMMENT     On May 4, 2000 this sequence version replaced gi:238292.
            Method: conceptual translation supplied by author.
FEATURES             Location/Qualifiers
     source          1..10
                     /organism="Homo sapiens"
                     /db_xref="taxon:9606"
     Protein         <1..>10
                     /product="cystic fibrosis transmembrane conductance
                     regulator"
                     /note="CFTR"
     CDS             1..10
                     /gene="CFTR"
                     /coded_by="S64643.1:<1..>30"
                     /note="conceptual translation presented here differs from
                     translation in publication"
ORIGIN
        1 tikenifgvs
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L8: Entry 5 of 13 File: USPT Mar 13, 2001

US-PAT-NO: 6201107
DOCUMENT-IDENTIFIER: US 6201107 B1

TITLE: Cystic fibrosis gene

DATE-ISSUED: March 13, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lap-Chee; Tsui	Toronto			CA
Riordan; John R.	Toronto			CA
Collins; Francis S.	Ann Arbor	MI		
Rommens; Johanna M.	Willowdale			CA
Iannuzzi; Michael C.	Ann Arbor	MI		
Kerem; Bat-Sheva	Toronto			CA
Drumm; Mitchell L.	Ann Arbor	MI		
Buchwald; Manuel	Toronto			CA

US-CL-CURRENT: 530/387.1; 435/344, 530/388.2, 530/389.2

CLAIMS:

What is claimed is:

1. An anti-CFTR polyclonal or monoclonal antibody specific for a normal CFTR polypeptide (SEQ ID NO:17), wherein said antibody is specific for an epitope of the sequence of SEQ ID NO:17 between amino acid residue positions 1 and 1480.

2. An anti-CFTR polyclonal ormonoclonal antibody specific for a mutant CFTR polypeptide, wherein said antibody is specific for an epitope of the sequence of SEQ ID NO:17 between amino acid residue positions 1 and 1480, wherein said amino acid sequence includes at least one cystic fibrosis (CF) mutation, wherein said cystic fibrosis (CF) mutation is a .DELTA.F508 mutation resulting from a three base pair deletion of the codon encoding phenylalanine at amino acid residue position 508 of the sequence of SEQ ID NO: 17.

3. A hybridoma producing a monoclonal antibody according to claim 2.

4. A hybridoma producing a monoclonal antibody according to claim 1.

Hit List

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Search Results - Record(s) 1 through 10 of 13 returned.

☐ 1. Document ID: US 6984487 B1

L8: Entry 1 of 13 File: USPT Jan 10, 2006

US-PAT-NO: 6984487
DOCUMENT-IDENTIFIER: US 6984487 B1

TITLE: Cystic fibrosis gene

DATE-ISSUED: January 10, 2006

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Tsui; Lap-Chee	Toronto			CA
Riordan; John R.	Toronto			CA
Collins; Francis S.	Ann Arbor	MI		US
Rommens; Johanna M.	Willowdale			CA
Iannuzzi; Michael C.	Ann Arbor	MI		US
Kerem; Bat-Sheva	Toronto			CA
Drumm; Mitchell L.	Ann Arbor	MI		US
Buchwald; Manuel	Toronto			CA

US-CL-CURRENT: 435/6; 530/350, 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

☐ 2. Document ID: US 6902907 B1

L8: Entry 2 of 13 File: USPT Jun 7, 2005

US-PAT-NO: 6902907
DOCUMENT-IDENTIFIER: US 6902907 B1

TITLE: Cystic fibrosis gene

DATE-ISSUED: June 7, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Tsui; Lap-Chee	Toronto			CA
Riordan; John R.	Toronto			CA
Collins; Francis S.	Ann Arbor	MI		
Rommens; Johanna M.	Willowdale			CA
Iannuzzi; Michael C.	Ann Arbor	MI		

Kerem; Bat-Sheva	Toronto		CA
Drumm; Mitchell L.	Ann Arbor	MI	
Buchwald; Manuel	Toronto		CA

US-CL-CURRENT: 435/69.1; 435/252.3, 435/320.1, 435/325, 530/350, 536/23.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc | Image

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☐ 3. Document ID: US 6730777 B1

L8: Entry 3 of 13 File: USPT May 4, 2004

US-PAT-NO: 6730777
DOCUMENT-IDENTIFIER: US 6730777 B1

TITLE: Cystic fibrosis gene

DATE-ISSUED: May 4, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Tsui; Lap-Chee	Toronto			CA
Riordan; John R.	Toronto			CA
Collins; Francis S.	Ann Arbor	MI		
Rommens; Johanna M.	Willowdale			CA
Iannuzzi; Michael C.	Ann Arbor	MI		
Kerem; Bat-Sheva	Toronto			CA
Drumm; Mitchell L.	Ann Arbor	MI		
Buchwald; Manuel	Toronto			CA

US-CL-CURRENT: 530/350

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc | Image

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☐ 4. Document ID: US 6207195 B1

L8: Entry 4 of 13 File: USPT Mar 27, 2001

US-PAT-NO: 6207195
DOCUMENT-IDENTIFIER: US 6207195 B1
** See image for Certificate of Correction **

TITLE: Therapeutic nanospheres

DATE-ISSUED: March 27, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Walsh; Scott	Owings Mills	MD		
Rubenstein; Ronald	Baltimore	MD		
Zeitlin; Pam	Baltimore	MD		

Leong; Kam W.	Ellicot City	MD

US-CL-CURRENT: 424/489; 435/320.1, 435/325, 435/455, 435/458, 514/44, 977/884, 977/906, 977/915, 977/920, 977/923

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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☐ 5. Document ID: US 6201107 B1

L8: Entry 5 of 13 File: USPT Mar 13, 2001

US-PAT-NO: 6201107
DOCUMENT-IDENTIFIER: US 6201107 B1

TITLE: Cystic fibrosis gene

DATE-ISSUED: March 13, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Lap-Chee; Tsui	Toronto			CA
Riordan; John R.	Toronto			CA
Collins; Francis S.	Ann Arbor	MI		
Rommens; Johanna M.	Willowdale			CA
Iannuzzi; Michael C.	Ann Arbor	MI		
Kerem; Bat-Sheva	Toronto			CA
Drumm; Mitchell L.	Ann Arbor	MI		
Buchwald; Manuel	Toronto			CA

US-CL-CURRENT: 530/387.1; 435/344, 530/388.2, 530/389.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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☐ 6. Document ID: US 6027880 A

L8: Entry 6 of 13 File: USPT Feb 22, 2000

US-PAT-NO: 6027880
DOCUMENT-IDENTIFIER: US 6027880 A

TITLE: Arrays of nucleic acid probes and methods of using the same for detecting cystic fibrosis

DATE-ISSUED: February 22, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cronin; Maureen T.	Los Altos	CA		
Miyada; Charles Garrett	San Jose	CA		
Hubbell; Earl A.	Mountain View	CA		
Chee; Mark	Palo Alto	CA		

Fodor; Stephen P. A.	Palo Alto	CA
Huang; Xiaohua C.	Mountain View	CA
Lipshutz; Robert J.	Palo Alto	CA
Lobban; Peter E.	Palo Alto	CA
Morris; Macdonald S.	Felton	CA
Sheldon; Edward L.	San Diego	CA

US-CL-CURRENT: 435/6; 422/50, 422/68.1, 436/501, 536/25.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc | Image

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☐ 7. Document ID: US 6001588 A

L8: Entry 7 of 13 File: USPT Dec 14, 1999

US-PAT-NO: 6001588
DOCUMENT-IDENTIFIER: US 6001588 A
**** See image for Certificate of Correction ****

TITLE: Introns and exons of the cystic fibrosis gene and mutations thereof

DATE-ISSUED: December 14, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Tsui; Lap-Chee	Toronto			CA
Rommens; Johanna M.	Willowdale			CA
Kerem; Bat-sheva	Jerusalem			IL

US-CL-CURRENT: 435/69.1; 435/252.3, 435/320.1, 536/23.5, 536/24.31

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Desc | Image

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☐ 8. Document ID: US 5981178 A

L8: Entry 8 of 13 File: USPT Nov 9, 1999

US-PAT-NO: 5981178
DOCUMENT-IDENTIFIER: US 5981178 A
**** See image for Certificate of Correction ****

TITLE: Methods for screening for mutations at various positions in the introns and exons of the cystic fibrosis gene

DATE-ISSUED: November 9, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Tsui; Lap-Chee	Toronto			CA
Rommens; Johanna M.	Willowdale			CA
Kerem; Bat-sheva	Jerusalem			IL

US-CL-CURRENT: 435/6; 435/810, 514/851, 536/24.31

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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☐ 9. Document ID: US 5834421 A

L8: Entry 9 of 13 File: USPT Nov 10, 1998

US-PAT-NO: 5834421
DOCUMENT-IDENTIFIER: US 5834421 A

TITLE: Methods and compositions for treating cystic fibrosis

DATE-ISSUED: November 10, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Cheng; Seng Hing	Wellesley	MA		
Jiang; Canwen	Marlboro	MA		

US-CL-CURRENT: 514/2; 514/540, 514/588, 514/619, 560/33, 564/160, 564/161, 564/192, 564/59

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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☐ 10. Document ID: US 5776677 A

L8: Entry 10 of 13 File: USPT Jul 7, 1998

US-PAT-NO: 5776677
DOCUMENT-IDENTIFIER: US 5776677 A

TITLE: Methods of detecting cystic fibrosis gene by nucleic acid hybridization

DATE-ISSUED: July 7, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Tsui; Lap-Chee	Toronto			CA
Riordan; John R.	Toronto			CA
Collins; Francis S.	Ann Arbor	MI		
Rommens; Johanna M.	Willowdale			CA
Iannuzzi; Michael C.	Ann Arbor	MI		
Kerem; Bat-Sheva	Toronto			CA
Drumm; Mitchell L.	Ann Arbor	MI		
Buchwald; Manuel	Toronto			CA

US-CL-CURRENT: 435/6; 435/91.2, 536/23.2, 536/24.3, 536/24.33

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Desc | Image

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Terms	Documents
mutant CFTR.clm.	13

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DATE: Monday, October 02, 2006

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☐	L12	Ll7 and internalizing peptide	0
☐	L11	L9 and internal peptide	0
☐	L10	L9 and internalizing peptide	0
☐	L9	6001588	2
☐	L8	mutant CFTR.clm.	13
☐	L7	mutant CFTR	79
☐	L6	gene encoding cystic fibrosis transmembrane conductance regulator	39
☐	L5	L2 and mutation? and dna	442
☐	L4	L2 and mutation?	450
☐	L3	cystic fibrosis transmembrane conductance regulator gene.clm.	7
☐	L2	L1 and amino acid sequence	534
☐	L1	cystic fibrosis transmembrane conductance regulator	924

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=> s internalizing peptide and Mutant CFTR
L1             0 INTERNALIZING PEPTIDE AND MUTANT CFTR

=> s  (CFTR or cystic fibrosis transmembrane conductance regulator) and homolog?
L2           765 (CFTR OR CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR)
                 AND HOMOLOG?

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3           424 DUP REM L2 (341 DUPLICATES REMOVED)

=> s l3 (rat or human or rabbit or mouse or animal?)
MISSING OPERATOR 'L13 (RAT'
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=> s l3 and (rat or human or rabbit or mouse or animal?)
L4           392 L3 AND (RAT OR HUMAN OR RABBIT OR MOUSE OR ANIMAL?)

=> s l4 and (mutant or mutation? variant?)
L5            44 L4 AND (MUTANT OR MUTATION? VARIANT?)

=> d l5 1-9 ibib ab

L5   ANSWER 1 OF 44     MEDLINE on STN
ACCESSION NUMBER:   2005657059     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 16234241
TITLE:              ATPase activity of p97/valosin-containing protein is
                    regulated by oxidative modification of the evolutionally
                    conserved cysteine 522 residue in Walker A motif.
AUTHOR:             Noguchi Masakatsu; Takata Takahiro; Kimura Yoko; Manno
                    Atsushi; Murakami Katsuhiro; Koike Masaaki; Ohizumi
                    Hiroshi; Hori Seiji; Kakizuka Akira
CORPORATE SOURCE:   Laboratory of Functional Biology, Kyoto University Graduate
                    School of Biostudies and Solution Oriented Research for
                    Science and Technology (JST), Kyoto 606-8501, Japan.
SOURCE:             The Journal of biological chemistry, (2005 Dec 16) Vol.
                    280, No. 50, pp. 41332-41.  Electronic Publication:
                    2005-10-18.
                    Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY:       United States
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
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ENTRY MONTH: 200602
ENTRY DATE: Entered STN: 18 Dec 2005
Last Updated on STN: 8 Feb 2006
Entered Medline: 7 Feb 2006

AB Valosin-containing protein (p97/VCP) has been proposed as playing crucial roles in a variety of physiological and pathological processes such as cancer and neurodegeneration. We previously showed that VCP(K524A), an ATPase activity-negative VCP mutant, induced vacuolization, accumulation of ubiquitinated proteins, and cell death, phenotypes commonly observed in neurodegenerative disorders. However, any regulatory mechanism of its ATPase activity has not yet been clarified. Here, we show that oxidative stress readily inactivates VCP ATPase activity. With liquid chromatography/tandem mass spectrometry, we found that at least three cysteine residues were modified by oxidative stress. Of them, the 522nd cysteine (Cys-522) was identified as the site responsible for the oxidative inactivation of VCP. VCP(C522T), a single-amino acid substitution mutant from cysteine to threonine, conferred almost complete resistance to the oxidative inactivation. In response to oxidative stress, VCP strengthened the interaction with Npl4 and Ufd1, both of which are essential in endoplasmic reticulum-associated protein degradation. Cys-522 is located in the second ATP binding motif and is highly conserved in multicellular but not unicellular organisms. Cdc48p (yeast VCP) has threonine in the corresponding amino acid, and it showed resistance to the oxidative inactivation in vitro. Furthermore, a yeast mutant (delta cdc48 + cdc48[T532C]) was shown to be susceptible to oxidants-induced growth inhibition and cell death. These results clearly demonstrate that VCP ATPase activity is regulated by the oxidative modification of the Cys-522 residue. This regulatory mechanism may play a key role in the conversion of oxidative stress to endoplasmic reticulum stress response in multicellular organisms and also in the pathological process of various neurodegenerative disorders.

L5 ANSWER 2 OF 44 MEDLINE on STN
ACCESSION NUMBER: 2005088226 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15719171
TITLE: Binding site of activators of the cystic fibrosis transmembrane conductance regulator in the nucleotide binding domains.
AUTHOR: Moran O; Galietta L J V; Zegarra-Moran O
CORPORATE SOURCE: Istituto di Biofisica, CNR, Via DeMarini 6, 16149 Genoa, Italy.. moran@ge.ibf.cnr.it
SOURCE: Cellular and molecular life sciences : CMLS, (2005 Feb) Vol. 62, No. 4, pp. 446-60.
Journal code: 9705402. ISSN: 1420-682X.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200503
ENTRY DATE: Entered STN: 19 Feb 2005
Last Updated on STN: 31 Mar 2005
Entered Medline: 30 Mar 2005

AB The use of substances that could activate the defective chloride channels of the mutant cystic fibrosis transmembrane conductance regulator (CFTR) has been suggested as possible therapy for cystic fibrosis. Using epithelia formed by cells stably transfected with wildtype or mutant (G551D, G1349D) CFTR, we estimated the apparent dissociation constant, K(D), of a series of CFTR activators by measuring the increase in the apical membrane current. Modification of apparent K(D) of CFTR activators by mutations of the nucleotide-binding domains (NBDs) suggests that the binding site might be in these regions. The human NBD structure was predicted by homology with murine NBD1. An NBD1-NBD2 complex was constructed

by overlying monomers to a bacterial ABC transporter NBD dimer in the "head-to-tail" conformation. Binding sites for CFTR activators were predicted by molecular docking. Comparison of theoretical binding free energy estimated in the model to free energy estimated from the apparent dissociation constants, K(D), resulted in a remarkably good correlation coefficient for one of the putative binding sites, located in the interface between NBD1 and NBD2.

L5 ANSWER 3 OF 44 MEDLINE on STN
ACCESSION NUMBER: 2004505132 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15246977
TITLE: Role of Cftr genotype in the response to chronic Pseudomonas aeruginosa lung infection in mice.
AUTHOR: van Heeckeren Anna M; Schluchter Mark D; Drumm Mitchell L; Davis Pamela B
CORPORATE SOURCE: Department of Pediatrics, Case Western Reserve University School of Medicine, Cleveland, Ohio 44106-4948, USA.. anna.vanheeckeren@case.edu
CONTRACT NUMBER: HL-60293 (NHLBI)
P30 DK-27651 (NIDDK)
SOURCE: American journal of physiology. Lung cellular and molecular physiology, (2004 Nov) Vol. 287, No. 5, pp. L944-52. Electronic Publication: 2004-07-09. Journal code: 100901229. ISSN: 1040-0605.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 13 Oct 2004
Last Updated on STN: 19 Dec 2004
Entered Medline: 19 Nov 2004

AB Patients with cystic fibrosis have a lesion in the cystic fibrosis transmembrane conductance regulator gene (CFTR), which is associated with abnormal regulation of other ion channels, abnormal glycosylation of secreted and cell surface molecules, and vulnerability to bacterial infection and inflammation in the lung usually leading to the death of these patients. The exact mechanism(s) by which mutation in CFTR leads to lung infection and inflammation is not clear. Mice bearing different mutations in the murine homolog to CFTR (Cftr) (R117H, S489X, Y122X, and DeltaF508, all backcrossed to the C57BL/6J background) were compared with respect to growth and in their ability to respond to lung infection elicited with Pseudomonas aeruginosa-laden agarose beads. Body weights of mice bearing mutations in Cftr were significantly smaller than wild-type mice at most ages. The inflammatory responses to P. aeruginosa-laden agarose beads were comparable in mice of all four Cftr mutant genotypes with respect to absolute and relative cell counts in bronchoalveolar lavage fluid, and cytokine levels (TNF-alpha, IL-1beta, IL-6, macrophage inflammatory protein-2, and keratinocyte chemoattractant) and eicosanoid levels (PGE2 and LTB4) in epithelial lining fluid: the few small differences observed occurred only between cystic fibrosis mice bearing the S489X mutation and those bearing the knockout mutation Y122X. Thus we cannot implicate either misprocessing of CFTR or failure of CFTR to reach the plasma membrane in the genesis of the excess inflammatory response of CF mice. Therefore, it appears that any functional defect in CFTR produces comparable inflammatory responses to lung infections with P. aeruginosa.

L5 ANSWER 4 OF 44 MEDLINE on STN
ACCESSION NUMBER: 2004325004 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15225287
TITLE: Disruption of AtMRP4, a guard cell plasma membrane ABCC-type ABC transporter, leads to deregulation of

stomatal opening and increased drought susceptibility.

AUTHOR: Klein Markus; Geisler Markus; Suh Su Jeoung; Kolukisaoglu H Uner; Azevedo Louis; Plaza Sonia; Curtis Mark D; Richter Andreas; Weder Barbara; Schulz Burkhard; Martinoia Enrico

CORPORATE SOURCE: Zurich Basel Plant Science Center, University of Zurich, Plant Biology, Zollikerstrasse 107, CH-8008 Zurich, Switzerland.. markus.klein@botinst.unizh.ch

SOURCE: The Plant journal : for cell and molecular biology, (2004 Jul) Vol. 39, No. 2, pp. 219-36.
Journal code: 9207397. ISSN: 0960-7412.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200409

ENTRY DATE: Entered STN: 1 Jul 2004
Last Updated on STN: 23 Sep 2004
Entered Medline: 22 Sep 2004

AB ATP-binding cassette (ABC) transporters are membrane proteins responsible for cellular detoxification processes in plants and animals. Recent evidence shows that this class of transporters may also be involved in many other cellular processes. Because of their homology with human multidrug resistance-associated proteins (MRP), cystic fibrosis transmembrane conductance regulator (CFTR) and sulfonylurea receptor (SUR), some plant ABC transporters have been implicated in the regulation of ion channel activities. This paper describes an investigation of the AtMRP4 gene and its role in stomatal regulation. Reporter gene studies showed that AtMRP4 is highly expressed in stomata and that the protein is localized to the plasma membrane. Stomatal aperture in three independent atmrp4 mutant alleles was larger than in wild-type plants, both in the light and in the dark, resulting in increased water loss but no change in the photosynthetic rate. In baker's yeast, AtMRP4 shows ATP-dependent, vanadate-sensitive transport of methotrexate (MTX), an antifolate and a substrate of mammalian MRPs. Treatment with MTX reduced stomatal opening in wild-type plants, but had no effect in atmrp4 mutants. These results indicate the involvement of AtMRP4 in the complex regulation of stomatal aperture.

L5 ANSWER 5 OF 44 MEDLINE on STN

ACCESSION NUMBER: 2004131617 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15024729

TITLE: Genomic rearrangements in the CFTR gene: extensive allelic heterogeneity and diverse mutational mechanisms.

AUTHOR: Audrezet Marie-Pierre; Chen Jian-Min; Raguenes Odile; Chuzhanova Nadia; Giteau Karine; Le Marechal Cedric; Quere Isabelle; Cooper David N; Ferec Claude

CORPORATE SOURCE: INSERM U613, Genetique Moleculaire et Genetique Epidemiologique, Centre Hospitalier Universitaire, Brest, France.

SOURCE: Human mutation, (2004 Apr) Vol. 23, No. 4, pp. 343-57.
Journal code: 9215429. E-ISSN: 1098-1004.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

OTHER SOURCE: OMIM-219700; OMIM-602421

ENTRY MONTH: 200405

ENTRY DATE: Entered STN: 17 Mar 2004
Last Updated on STN: 10 May 2004
Entered Medline: 6 May 2004

AB Cystic fibrosis (CF) is caused by mutations in the cystic fibrosis transmembrane conductance regulator gene (CFTR/ABCC7). Despite the extensive and

enduring efforts of many CF researchers over the past 14 years, up to 30% of disease alleles still remain to be identified in some populations. It has long been suggested that gross genomic rearrangements could account for these unidentified alleles. To date, however, only a few large deletions have been found in the CFTR gene and only three have been fully characterized. Here, we report the first systematic screening of the 27 exons of the CFTR gene for large genomic rearrangements, by means of the quantitative multiplex PCR of short fluorescent fragments (QMPSF). A well-characterized cohort of 39 classical CF patients carrying at least one unidentified allele (after extensive and complete screening of the CFTR gene by both denaturing gradient gel electrophoresis and denaturing high-performance liquid chromatography) participated in this study. Using QMPSF, some 16% of the previously unidentified CF mutant alleles were identified and characterized, including five novel mutations (one large deletion and four indels). The breakpoints of these five mutations were precisely determined, enabling us to explore the underlying mechanisms of mutagenesis. Although non-homologous recombination may be invoked to explain all five complex lesions, each mutation appears to have arisen through a different mechanism. One of the indels was highly unusual in that it involved the insertion of a short 41 bp sequence with partial homology to a retrotranspositionally-competent LINE-1 element. The insertion of this ultra-short LINE-1 element (dubbed a "hyphen element") may constitute a novel type of mutation associated with human genetic disease.

L5 ANSWER 6 OF 44 MEDLINE on STN
ACCESSION NUMBER: 2004003003 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14698290
TITLE: The rad50 signature motif: essential to ATP binding and biological function.
AUTHOR: Moncalian Gabriel; Lengsfeld Bettina; Bhaskara Venugopal; Hopfner Karl-Peter; Karcher Annette; Alden Erinn; Tainer John A; Paull Tanya T
CORPORATE SOURCE: The Scripps Research Institute, 10550 North Torrey Pines Rd., MB4, La Jolla, CA 92037, USA.
CONTRACT NUMBER: P01 CA92584 (NCI)
R01 CA94008-01 (NCI)
SOURCE: Journal of molecular biology, (2004 Jan 23) Vol. 335, No. 4, pp. 937-51.
Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1US8
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 6 Jan 2004
Last Updated on STN: 11 Feb 2004
Entered Medline: 10 Feb 2004

AB The repair of double-strand breaks in DNA is an essential process in all organisms, and requires the coordinated activities of evolutionarily conserved protein assemblies. One of the most critical of these is the Mre11/Rad50 (M/R) complex, which is present in all three biological kingdoms, but is not well-understood at the biochemical level. Previous structural analysis of a Rad50 homolog from archaebacteria illuminated the catalytic core of the enzyme, an ATP-binding domain related to the ABC transporter family of ATPases. Here, we present the crystallographic structure of the Rad50 mutant S793R. This missense signature motif mutation changes the key serine residue in the signature motif that is conserved among Rad50 homologs and ABC ATPases. The S793R mutation is analogous to the mutation S549R in the cystic fibrosis transmembrane conductance regulator (CFTR) that results in

cystic fibrosis. We show here that the serine to arginine change in the Rad50 protein prevents ATP binding and disrupts the communication among the other ATP-binding loops. This structural change, in turn, alters the communication between Rad50 monomers and thus prevents Rad50 dimerization. The equivalent mutation was made in the human Rad50 gene, and the resulting mutant protein did form a complex with Mre11 and Nbs1, but was specifically deficient in all ATP-dependent enzymatic activities. This signature motif structure-function homology extends to yeast, because the same mutation introduced into the Saccharomyces cerevisiae RAD50 gene generated an allele that failed to complement a rad50 deletion strain in DNA repair assays in vivo. These structural and biochemical results extend our understanding of the Rad50 catalytic domain and validate the use of the signature motif mutant to test the role of Rad50 ATP binding in diverse organisms.

L5 ANSWER 7 OF 44 MEDLINE on STN
ACCESSION NUMBER: 2003404079 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12907241
TITLE: Inhibition of ATP-sensitive K+ channels by substituted benzo[c]quinolizinium CFTR activators.
AUTHOR: Prost Ann- Lise; Derand Renaud; Gros Laurent; Becq Frederic; Vivaudou Michel
CORPORATE SOURCE: CEA, DRDC, Laboratoire de Biophysique Moleculaire et Cellulaire (UMR 5090), 17 rue des Martyrs, 38054 Grenoble, France.
SOURCE: Biochemical pharmacology, (2003 Aug 1) Vol. 66, No. 3, pp. 425-30.
Journal code: 0101032. ISSN: 0006-2952.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200309
ENTRY DATE: Entered STN: 29 Aug 2003
Last Updated on STN: 13 Sep 2003
Entered Medline: 12 Sep 2003

AB The substituted benzo[c]quinolizinium compounds MPB-07 and MPB-91 are novel activators of the cystic fibrosis transmembrane conductance regulator (CFTR) chloride channel. High homologies between CFTR and the sulfonylurea receptor (SUR), which associates with the potassium channel Kir6.2 to form the ATP-sensitive K(+) (K(ATP)) channel, prompted us to examine possible effects of these compounds on K(ATP) channels using electrophysiological recordings and binding assays. Activity of recombinant K(ATP) channels expressed in Xenopus oocytes was recorded in the inside-out configuration of the patch-clamp technique. Channels were practically unaffected by MPB-07 but were fully blocked by MPB-91 with half-inhibition achieved at approximately 20 microM MPB-91. These effects were similar on channels formed by Kir6.2, and either the SUR1 or SUR2A isoforms were independent of the presence of nucleotides. They were not influenced by SUR mutations known to interfere with its nucleotide-binding capacity. MPB-91, but not MPB-07, was able to displace binding of glibenclamide to HEK cells expressing recombinant SUR1/Kir6.2 channels. Glibenclamide binding to native channels from pancreatic MIN6 cells was also displaced by MPB-91. A Kir6.2 mutant able to form channels without SUR was also blocked by MPB-91, but not by MPB-07. These observations demonstrate that neither MPB-07 nor MPB-91 interact with SUR, in spite of its high homology with CFTR, and that MPB-91 blocks K(ATP) channels by binding to the Kir6.2 subunit. Thus, caution should be exercised when planning to use MPB compounds in cystic fibrosis therapy, specially MPB-91 which could nonetheless find interesting applications as the precursor of a new class of K channel blockers.

L5 ANSWER 8 OF 44 MEDLINE on STN

ACCESSION NUMBER: 2002423268 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12082160
TITLE: A role for mammalian Ubc6 homologues in ER-associated protein degradation.
AUTHOR: Lenk Uwe; Yu Helen; Walter Jan; Gelman Marina S; Hartmann Enno; Kopito Ron R; Sommer Thomas
CORPORATE SOURCE: The Max-Delbruck-Centrum fur Molekulare Medizin, Robert-Rossle-Str. 10, 13092 Berlin, Germany.
SOURCE: Journal of cell science, (2002 Jul 15) Vol. 115, No. Pt 14, pp. 3007-14.
Journal code: 0052457. ISSN: 0021-9533.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 16 Aug 2002
Last Updated on STN: 28 Dec 2002
Entered Medline: 27 Dec 2002

AB Integral membrane and secretory proteins which fail to fold productively are retained in the endoplasmic reticulum and targeted for degradation by cytoplasmic proteasomes. Genetic and biochemical analyses suggest that substrates of this pathway must be dislocated across the membrane of the endoplasmic reticulum (ER) by a process requiring a functional Sec61 complex and multiubiquitinylation. In yeast, the tail-anchored ubiquitin-conjugating enzyme Ubc6p, which is localized to the cytoplasmic surface of the ER, participates in ER-associated degradation (ERAD) of misfolded proteins. Here we describe the identification of two families of mammalian Ubc6p-related proteins. Members of both families are also located in the ER membrane and display a similar membrane topology as the yeast enzyme. Furthermore we show that expression of elevated levels of wild-type and dominant-negative alleles of these components affects specifically ERAD of the alpha subunit of the T-cell receptor and a mutant form of the CFTR protein. Similarly, we describe that the expression level of Ubc6p in yeast is also critical for ERAD, suggesting that the Ubc6p function is highly conserved from yeast to mammals.

L5 ANSWER 9 OF 44 MEDLINE on STN
ACCESSION NUMBER: 2002290922 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12032687
TITLE: Isolation of CF cell lines corrected at DeltaF508-CFTR locus by SFHR-mediated targeting.
AUTHOR: Bruscia E; Sangiuolo F; Sinibaldi P; Goncz K K; Novelli G; Gruenert D C
CORPORATE SOURCE: Human Molecular Genetics, Department of Medicine, University of Vermont, VT 05405, USA.
SOURCE: Gene therapy, (2002 Jun) Vol. 9, No. 11, pp. 683-5.
Journal code: 9421525. ISSN: 0969-7128.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 29 May 2002
Last Updated on STN: 14 Aug 2002
Entered Medline: 13 Aug 2002

AB Cystic fibrosis is the most common inherited disease in the Caucasian population. About 70% of all CF chromosomes carry the DeltaF508 mutation, a 3-bp deletion that results in the loss of a phenylalanine at amino acid 508 in the CF transmembrane conductance regulator (CFTR) protein. Direct modification of the DeltaF508 locus of endogenous CFTR was achieved by small fragment homologous replacement (SFHR). Transformed human airway epithelial cells (CFBE41o(-)), homozygous for DeltaF508 mutation, were transfected with

small fragments (491-bp) of wild-type (WT) CFTR DNA comprising exon 10 and the flanking introns. The DNA fragments were in a liposome-DNA complex at a charge ratio of 6:1 (+:-), respectively). The population of transfected cells was subcloned by limiting dilution at approximately 1 cell/well in 96-well plates. Individual colonies were isolated and analyzed. The DNA from several colonies was characterized by radiolabeled, nonallele-specific and radiolabeled, allele-specific PCR amplification, as well as by genomic DNA fingerprinting. The CFTR -WT allele was detected in five of these colonies by allele-specific PCR amplification thus indicating that the cell lines carried both WT and DeltaF alleles. DNA fingerprint analysis confirmed that the colonies were isogenic and derived from the parental CFBE41o(-) cell line. Although, the WT allele was detected by allele-specific PCR, it was not detected initially when the same samples were analyzed by non allele-specific PCR. A sensitivity assay, mixing the genomic DNA of wild-type (16HBE14o(-)) and mutant (CFBE41o(-)) cell lines, indicated that the allele-specific PCR was at least 25-fold more sensitive than non allele-specific PCR. These results suggest that the colony is not yet clonal, but still contains a population of parental, CFBE41o(-) cells that have not been modified. Based on the mixing analysis, the proportion of corrected cells appears to be between 1 and 10% of the total population. Nonallele-specific reverse transcriptase PCR (RT-PCR) analysis of the CFTR mRNA indicated that two of the colonies expressed both WT and DeltaF508 CFTR mRNA, while one colony appeared to express only the WT mRNA. The mRNA results were confirmed by sequence analysis of 3' end primer extension products from the mRNA of CFTR exon 10 showing that the mRNA containing exon 10. Furthermore, a survey of primer extension products indicated no random insertion of the fragment in an expressed gene. This study demonstrates SFHR-mediated modification of the DeltaF508 allele in DeltaF508 homozygote human airway epithelial cells over multiple generations. The resultant cells express WT-CFTR mRNA and can be subcloned further to isolate isogenic clonal populations of cells.

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     02 OCT 2006
L1             0 S INTERNALIZING PEPTIDE AND MUTANT CFTR
L2           765 S  (CFTR OR CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR
L3           424 DUP REM L2 (341 DUPLICATES REMOVED)
L4           392 S L3 AND (RAT OR HUMAN OR RABBIT OR MOUSE OR ANIMAL?)
L5            44 S L4 AND (MUTANT OR MUTATION? VARIANT?)

=> s l5 and ( internal peptide or internalizing peptide)
L6             0 L5 AND (INTERNAL PEPTIDE OR INTERNALIZING PEPTIDE)

=> d his

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     02 OCT 2006
L1             0 S INTERNALIZING PEPTIDE AND MUTANT CFTR
L2           765 S  (CFTR OR CYSTIC FIBROSIS TRANSMEMBRANE CONDUCTANCE REGULATOR
L3           424 DUP REM L2 (341 DUPLICATES REMOVED)
L4           392 S L3 AND (RAT OR HUMAN OR RABBIT OR MOUSE OR ANIMAL?)
L5            44 S L4 AND (MUTANT OR MUTATION? VARIANT?)
L6             0 S L5 AND ( INTERNAL PEPTIDE OR INTERNALIZING PEPTIDE)

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                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

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=> s (Cystic fibrosis trans-membrane conductance regulator or CFTR) and amino acid sequenc
   2 FILES SEARCHED...
L1          622 (CYSTIC FIBROSIS TRANS-MEMBRANE CONDUCTANCE REGULATOR OR CFTR)
                AND AMINO ACID SEQUENCE

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=> dup rem l1
PROCESSING COMPLETED FOR L1
L2           493 DUP REM L1 (129 DUPLICATES REMOVED)

=> focus l2
PROCESSING COMPLETED FOR L2
L3           493 FOCUS L2 1-

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L3   ANSWER 1 OF 493  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         1998:137177  HCAPLUS
DOCUMENT NUMBER:          128:306702
TITLE:                    CFTR mRNA and its truncated splice variant
                          (TRN-CFTR) are differentially expressed
                          during collecting duct ontogeny
AUTHOR(S):                Huber, Stephan; Braun, Gerald; Burger-Kentischer,
                          Anke; Reinhart, Brigitte; Luckow, Bruno; Horster,
                          Michael
CORPORATE SOURCE:         Pettenkoferstr. 12, Physiologisches Institut,
                          Ludwig-Maximilians-Universitat, Munich, 80336, Germany
SOURCE:                   FEBS Letters (1998), 423(3), 362-366
                          CODEN: FEBLAL; ISSN: 0014-5793
PUBLISHER:                Elsevier Science B.V.
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   The collecting duct epithelium originates from the embryonic ureter by
     branching morphogenesis.  Ontogeny-dependent changes of CFTR
     mRNA expression were assessed by quant. reverse transcriptase-polymerase
     chain reaction (RT-PCR) in primary monolayer cultures of rat ureteric buds
     (UB) and cortical collecting ducts, microdissected at different embryonic
     and postnatal developmental stages.  The amt. of wild-type CFTR
     -specific PCR product in UB declined to 20 of the initial value between
     embryonic gestational day E15 and postnatal day P1.  After birth the
     CFTR product increased transiently between P1 and P7 by a factor
     of 10 and decreased towards day P14.  PCR products specific for TRN-
     CFTR, a truncated splice variant, however, were low in early
     embryonic cells, increased markedly between day E17 and P2, and reached a
     plateau postnatally.  Therefore, mRNA encoding TRN-CFTR does not
     appear to have a specific embryonic-morphogenetic function.  By contrast,
     such function is suggested for wild-type CFTR mRNA as its
     abundance was high in early embryonic nephrogenesis, as well as during a
     postnatal period shortly before branching morphogenesis is completed.
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REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d l3 2-10

L3 ANSWER 2 OF 493 MEDLINE on STN
AN 93122796 MEDLINE
DN PubMed ID: 1282491
TI Localization of the gene encoding the cystic fibrosis transmembrane conductance regulator (CFTR) in the rat to chromosome 4 and implications for the evolution of mammalian chromosomes.
AU Trezise A E; Szpirer C; Buchwald M
CS Department of Genetics, Hospital for Sick Children, Toronto, Ontario, Canada.
SO Genomics, (1992 Dec) Vol. 14, No. 4, pp. 869-74.
Journal code: 8800135. ISSN: 0888-7543.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-M89906
EM 199302
ED Entered STN: 26 Feb 1993
Last Updated on STN: 29 Jan 1996
Entered Medline: 10 Feb 1993

L3 ANSWER 3 OF 493 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:972178 HCAPLUS
DN 140:35946
TI CFTR modifier genes and expressed proteins, in particular Kir4.2, and their regulators, useful in treating cystic fibrosis and methods and products for detecting and/or identifying same
IN Whitsett, Jeffrey Allen; Aronow, Bruce Jefferson; Clark, Jean Cantwell
PA Children's Hospital Medical Center, USA
SO PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003102140	A2	20031211	WO 2003-US16896	20030530
	WO 2003102140	A3	20040610		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2488012	AA	20031211	CA 2003-2488012	20030530
	AU 2003238791	A1	20031219	AU 2003-238791	20030530
	EP 1513870	A2	20050316	EP 2003-734252	20030530
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	CN 1671734	A	20050921	CN 2003-818347	20030530
	JP 2005528449	T2	20050922	JP 2004-510382	20030530
	US 2005158747	A1	20050721	US 2004-999587	20041130
PRAI	US 2002-384855P	P	20020531		
	US 2002-384856P	P	20020531		
	WO 2003-US16896	W	20030530		

L3 ANSWER 4 OF 493 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:329918 HCAPLUS
DN 138:380206
TI Alternative 5' exons of the CFTR gene show developmental regulation
AU Mouchel, Nathalie; Broackes-Carter, Fiona; Harris, Ann
CS Paediatric Molecular Genetics, Weatherall Institute of Molecular Medicine, John Radcliffe Hospital, Oxford University, Oxford, OX3 9DS, UK
SO Human Molecular Genetics (2003), 12(7), 759-769
CODEN: HMGEE5; ISSN: 0964-6906
PB Oxford University Press
DT Journal
LA English
RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 493 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:265583 HCAPLUS
DN 134:291076
TI Materials and method for detecting CFTR dimerization, screening for compounds, restoring said dimerization, as potential drugs for cystic fibrosis
IN Teem, John L.
PA Florida State University Research Foundation, USA
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001025421	A2	20010412	WO 2000-US27900	20001006
	WO 2001025421	A3	20010830		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001011939	A5	20010510	AU 2001-11939	20001006
PRAI	US 1999-157996P	P	19991006		
	US 2000-181892P	P	20000211		
	US 2000-182373P	P	20000214		
	WO 2000-US27900	W	20001006		

L3 ANSWER 6 OF 493 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 1999:113799 HCAPLUS
DN 130:163964
TI DNA encoding glutathione transporter function of CFTR for gene therapy of cystic fibrosis
IN Lenoir, Gerard; Barthe, Joel; Lallemand, Jean-yves; Stoven, Veronique; Annereau, Jean-Philippe
PA Assistance Publique - Hopitaux de Paris, Fr.
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA French
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9906547	A2	19990211	WO 1998-FR1704	19980730

WO 9906547 A3 20000810
W: AU, CA, JP, PL, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
FR 2766841 A1 19990205 FR 1997-9829 19970731
CA 2298062 AA 19990211 CA 1998-2298062 19980730
AU 9889861 A1 19990222 AU 1998-89861 19980730
EP 1025222 A1 20000809 EP 1998-941505 19980730
R: DE, FR, GB, IT
JP 2001512010 T2 20010821 JP 2000-505288 19980730
PRAI FR 1997-9829 A 19970731
WO 1998-FR1704 W 19980730

L3 ANSWER 7 OF 493 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 1997:747736 HCAPLUS
DN 128:86851
TI Regulation of CFTR chloride channels by syntaxin and Munc18 isoforms
AU Naren, Anjaparavanda P.; Nelson, Deborah J.; Xie, Weiwen; Jovov, Biljana; Pevsner, Jonathan; Bennett, Mark K.; Benos, Dale J.; Quick, Michael W.; Kirk, Kevin L.
CS Dep. Physiol. Biophys., Gregory Fleming James Cystic Fibrosis Research Center, Univ. Alabama at Birmingham, Birmingham, AL, 35294, USA
SO Nature (London) (1997), 390(6657), 302-305
CODEN: NATUAS; ISSN: 0028-0836
PB Macmillan Magazines
DT Journal
LA English
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 493 HCAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:242135 HCAPLUS
DN 138:248553
TI Q4N2NEG2 peptides enhancing cystic fibrosis transmembrane conductance regulator (CFTR) activity and therapeutic use for cystic fibrosis
IN Davis, Pamela B.; Ma, Jianjie; Gerken, Thomas
PA Case Western Reserve University, USA
SO PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003024409	A2	20030327	WO 2002-US30094	20020923
US 2003100501	A1	20030529	US 2002-252012	20020923
PRAI US 2001-323724P	P	20010921		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

L3 ANSWER 9 OF 493 MEDLINE on STN
AN 1998070814 MEDLINE
DN PubMed ID: 9405675
TI Development of an epithelium-specific expression cassette with human DNA regulatory elements for transgene expression in lung airways.

AU Chow Y H; O'Brodovich H; Plumb J; Wen Y; Sohn K J; Lu Z; Zhang F; Lukacs G L; Tanswell A K; Hui C C; Buchwald M; Hu J
CS Division of Respiratory Research and Lung Gene Therapy Programme, University of Toronto, Toronto, ON, M5G 1X8 Canada.
SO Proceedings of the National Academy of Sciences of the United States of America, (1997 Dec 23) Vol. 94, No. 26, pp. 14695-700.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199802
ED Entered STN: 17 Feb 1998
Last Updated on STN: 17 Feb 1998
Entered Medline: 2 Feb 1998

L3 ANSWER 10 OF 493 MEDLINE on STN
AN 2004181051 MEDLINE
DN PubMed ID: 14754881
TI Cardiac expression of the cystic fibrosis transmembrane conductance regulator involves novel exon 1 usage to produce a unique amino-terminal protein.
AU Davies Wayne L; Vandenberg Jamie I; Sayeed Rana A; Trezise Ann E O
CS School of Biomedical Science, University of Queensland, Brisbane, Queensland 4072, Australia.
SO The Journal of biological chemistry, (2004 Apr 16) Vol. 279, No. 16, pp. 15877-87. Electronic Publication: 2004-01-30.
Journal code: 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AY256886; GENBANK-AY256887; GENBANK-AY256888; GENBANK-AY256889
EM 200407
ED Entered STN: 13 Apr 2004
Last Updated on STN: 23 Jul 2004
Entered Medline: 22 Jul 2004

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(FILE 'HOME' ENTERED AT 11:14:08 ON 02 OCT 2006)

FILE 'MEDLINE, HCAPLUS, EMBASE' ENTERED AT 11:14:33 ON 02 OCT 2006
L1 622 S (CYSTIC FIBROSIS TRANS-MEMBRANE CONDUCTANCE REGULATOR OR CFTR
L2 493 DUP REM L1 (129 DUPLICATES REMOVED)
L3 493 FOCUS L2 1-

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	35.80	36.01

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-0.75	-0.75

STN INTERNATIONAL LOGOFF AT 11:20:14 ON 02 OCT 2006

The vector, according to an aspect of this invention, is operatively linked to an expression control sequence in the recombinant DNA molecule so that the normal CFTR protein can be expressed, or alternatively with the other selected mutant DNA sequence the mutant CFTR polypeptide can be expressed. The expression control sequence is selected from the group consisting of sequences that control the expression of genes of prokaryotic or eukaryotic cells and their viruses and combinations thereof.

According to another aspect of the invention, a method for producing normal CFTR polypeptide comprises the steps of:

(a) culturing a host cell transfected with the recombinant vector for the normal DNA sequence in a medium and under conditions favorable for expression of the normal CFTR polypeptide; and

(b) isolating the expressed normal CFTR polypeptide.

According to another aspect of the invention, a method for producing a mutant CFTR polypeptide comprises the steps of:

(a) culturing a host cell transfected with the recombinant vector for the mutant DNA sequence in a medium and under conditions favorable for expression of the mutant CFTR polypeptide; and

(b) isolating the expressed mutant CFTR polypeptide.

According to another aspect of the invention, a purified protein of human cell membrane origin comprises an amino sequence encoded by the mutant DNA sequence where the protein, when present in human cell membrane, is associated with cell function which causes the genetic disease cystic fibrosis.

According to another aspect of the invention, the CFTR polypeptide is characterized by a molecular weight of about 170,000 daltons and an epithelial cell transmembrane ion conductance affecting activity.

According to another aspect of the invention, a substantially pure CFTR protein normally expressed in human epithelial cells and characterized by being capable of participating in regulation and in control of ion transport through epithelial cells by binding to spithelial cell membrane to modulate ion movement through channels formed in the epithelial cell membrane.

According to another aspect of the invention, a process for isolating the CFTR protein comprises:

(a) extracting peripheral proteins from membranes of epithelial cells to provide membrane material having integral proteins including said CFTR protein:

(b) solubilizing said integral proteins of said membrane material to form a solution of said integral proteins;

(c) separating said CFTR protein to remove any remaining other proteins of mammalian origin.

According to another aspect of the invention, a method is provided for screening a subject to determine if the subject is a CF carrier or a CF patient comprising the steps of providing a biological sample of the subject to be screened and providing an assay for detecting in the biological sample, the presence of at least a member from the group consisting of the normal CF gene, normal CF gene products, a mutant CF gene, mutant CF gene products and mixtures thereof.

According to another aspect of the invention, an immunologically active anti-CFTR polyclonal or monoclonal antibody specific for CFTR polypeptide is provided.

According to another aspect of the invention, a kit for assaying for the presence of a CF gene by immunoassay techniques comprises:

(a) an antibody which specifically binds to a gene product of the CF gene;

(b) reagent means for detecting the binding of the antibody to the gene product; and

(c) the antibody and reagent means each being present in amounts effective to perform the immunoassay.

According to another aspect of the invention, a kit for assaying for the presence of a CF gene by hybridization technique comprises:

(a) an oligonucleotide probe which specifically binds to the CF gene;

(b) reagent means for detecting the hybridization of the oligonucleotide probe to the CF gene; and

(c) the probe and reagent means each being present in amounts effective to perform the hybridization assay.

According to another aspect of the invention, a method is provided for treatment for cystic fibrosis in a patient. The treatment comprises the step of administering to the patient a therapeutically effective amount of the normal CFTR protein.

According to another aspect of the invention, a method of gene therapy for cystic fibrosis comprises the step of delivery of a DNA molecule which includes a sequence corresponding to the normal DNA sequence encoding for normal CFTR protein.

According to another aspect of the invention, an animal comprises an heterologous cell system. The cell system includes a recombinant cloning vector which includes the recombinant DNA sequence corresponding to the mutant DNA sequence which induces cystic fibrosis symptoms in the animal.

According to another aspect of the invention, a transgenic mouse exhibits cystic fibrosis symptoms.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is the nucleotide sequence of the CF gene and the amino acid sequence of the CFTR protein.

FIG. 2 is a restriction map of the CF gene and the schematic strategy used to chromosome walk and jump to the gene.

FIGS. 3A, 3B, 3C, 3D, and 3E are a pulse-field-gel electrophoresis map of the region including and surrounding the CF gene.

FIGS. 4A, 4B and 4C show the detection of conserved nucleotide sequences by cross-species hybridization.

FIG. 4D is a restriction map of overlapping segments of probes E4.3 and H1.6.

FIG. 5 is an RNA blot hybridization analysis, using genomic and cDNA probes. Hybridization to fibroblast, trachea (normal and CF), pancreas, liver, HL60, T84, and brain RNA is shown.

FIG. 6 is the methylation status of the E4.3 cloned region at the 5' and of the CF gene.

FIG. 7 is a restriction map of the CFTR cDNA showing alignment of the cDNA to the genomic DNA 30 fragments.

FIG. 8 is an RNA gel blot analysis depicting hybridization by a portion of the CFTR cDNA (clone 10-1) to a 6.5 kb mRNA transcript in various human tissues.

FIGS. 9A, 9B, 9C, and 9D are is a DNA blot hybridization analysis depicting hybridization by the CFTR cDNA clones to genomic DNA digested with EcoRI and HindIII.

FIGS. 10A, 10B, and 10C are is a primer extension experiment characterizing the 5' and 3' ends of the CFTR cDNA.